Citation:

Weiss A, Beloosesky Y, Boaz M, Yalov A, Kornowski R, Grossman E. Body mass index is inversely related to mortality in elderly subjects. *J Gen Intern Med.* 2008; 23: 19-24.

PubMed ID: 17955304

Study Design:

Retrospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To identify the long-term effect of overweight on mortality in adults age 60 years and older.

Inclusion Criteria:

- Age 60 years or older
- Admitted to a geriatric ward between January 1, 1999 and December 31, 2000
- Participation in a different study for orthostatic hypotension
- Willing and able to stand for height, weight and blood pressure measurement
- Study procedures were approved by the institutional and Ministry of Health Ethics Committees.

Exclusion Criteria:

- Age less than 60 years
- Unwilling or unable to stand for height, weight and blood pressure measurement.

Description of Study Protocol:

Recruitment

- Consecutive admissions (January 1, 1999 to December 31, 2000) of individuals age 60 years or older to an acute geriatric ward were screened for participation in a study on orthostatic hypotension
- This study follows up on those participants until August 31, 2004.

Design

This retrospective cohort design used medical record and death certificate reviews to ascertain

health characteristics upon hospital admission and possible mortality by the end of the follow up period.

Blinding

Medical records review was blinded.

Statistical Analysis

- Baseline characteristics were compared by body mass index (BMI) quartile and survival status, using ANOVA and post-hoc pairwise testing with a Bonferroni correction ($P<0.0026$) or chi-square test
- Age-adjusted mortality rates were compared by BMI quartile and Kaplan-Meier curves with log rank or Wilcoxon test
- Cox proportional hazard regression was used to model survival. Regression was performed in a forward stepwise manner, with variables entered for $P<0.15$ and retained only if $P<0.05$ after subsequent variables were entered.

Data Collection Summary:

Timing of Measurements

- Baseline characteristics were measured upon hospital admission (January 1, 1999 to December 31, 2000)
- Mortality was assessed through August 31, 2004.

Dependent Variables

- Mortality (obtained from death certificates maintained by the Ministry of Interior Affairs Population Registry and hospital medical records)
- Cause of death: Cardiovascular causes included stroke, myocardial infarction (MI), congestive heart failure (CHF), sudden death, aortic aneurysm rupture, arrhythmia or other thromboembolic event.

Independent Variables

- Age
- Sex
- Standing height (measured to nearest 0.5cm)
- Weight (measured to nearest 0.5kg)
- BMI (kg/m^2); BMI quartiles:
    - Less than 22
    - 22 to 25
    - 25.01 to 28
    - 28 or more
- Standing blood pressure
- Ethnic origin
- Reason for hospital admission
- Diagnoses
- Prescribed medications
- Laboratory findings: Complete blood cell count and chemistry, serum glucose, urea, creatinine, sodium, potassium, thyrotropin, vitamin B_{12}, folic acid

- Comorbidities
  - Hypertension (prescription for anti-hypertensives in medical record or blood pressure higher than 140/90mmHg on two or more measurements)
  - Diabetes mellitus (prescription for hypoglycemics in medical record or fasting blood glucose of 126mg per dL on two or more measurements)
  - Renal failure (serum creatinine more than 1.5mg per dL on two or more measurements)
  - Ischemic heart disease
  - CHF
  - Parkinson's.

Description of Actual Data Sample:

- *Initial N:* 1,852 screened: 502 were eligible and 1,350 either could not stand or did not cooperate; of the 502, 32 were lost to follow-up or missing data
- *Attrition (final N):* 470 (25% of cases screened and 94% of eligible cases)
- *Mean age:* 81.5±6.8 years
- *Other relevant demographics:* 51.9% female; age, sex and duration of hospital stay did not differ between participants and non-participants
- *Anthropometrics:*
  - Mean BMI 25.2±4.5kg/m^2 (range: 15.0 to 42.2)
  - Subjects in the higher BMI quartiles were significantly older, had higher systolic and diastolic blood pressure and were more likely to have a diagnosis of HTN, were more likely to have prescription for diuretics or beta blockers, and were less likely to have a diagnosis of Parkinson's
- *Location:* Israel.

Summary of Results:

- Of the 470 cases in the cohort, 248 died during the follow-up period (mean 3.5 years; median 4.2 years; range 1.6 to 5.3 years)
  - Causes of death included cardiovascular disease (51%), sepsis (45%) and malignancy (14%), with some death certificates listing more than one cause
  - Men were more likely to die from cardiovascular causes (P=0.04)
- Overall mortality rate was 15.3 per 100 person-years
- Survivors had higher BMI at baseline (P<0.0001). Those who died were more likely to be male or have ischemic heart disease, CHF, diabetes mellitus, Parkinson's disease or have more than one disease (see table).

Characteristics (mean ± SD)	Alive (N=222)	Dead (N=248)	P-value
Age (years)	79.4±6.4	83.4±6.6	0.40
Percentage female	57.7	46.8	0.02
BMI	26.3±4.6	24.1±4.2	<0.01
Comorbidities (percentage)			
Hypertension	64	62	0.70
Diabetes mellitus	31	42	0.04
Ischemic heart disease	52	62	0.03
Congestive heart failure	23	38	<0.01

Stroke	31	33	0.60
Renal failure	17	31	<0.01
Chronic lung disease	19	26	0.10
Parkinson's disease	8	17	<0.01
More than one disease	95	98	0.04

From the lowest to highest BMI quartile, age-adjusted mortality rate decreased significantly (P<0.01):

BMI Quartile (kg/m^2)	Number of Cases	Number of Deaths	Mortality per 100 Patient-years	Age-adjusted Mortality per 100 Patient-years
Less than 22	109	75	25.5	24.0
22 to 25	131	72	15.4	15.4
25.01 to 28	118	62	15.1	15.4
28 or more	112	39	8.9	9.6

- The same pattern was observed when excluding those with acute disease (i.e., died within six months of hospitalization; N=42).

Other Findings

In multivariable Cox proportional hazards regression models, the following increased risk of all-cause mortality:

- Male, older age, diabetes mellitus and renal failure
- Highest BMI quartile decreased risk by a relative 33% (95% CI: 13% to 49%).

Author Conclusion:

- In a retrospective cohort study of elderly adults admitted to an acute hospital ward, increased BMI was associated with lower mortality in a linear fashion. The association held for both sexes and all causes of death
    - The effect may be due to preservation of fat-free mass in older adults by protecting against disease-related catabolism, or may be related to effects on the inflammatory system or in maintaining a metabolic reserve
    - The findings are similar to another large-scale observational study of older adults, but are in contrast to findings that BMI is associated with increased mortality among young and middle-age individuals
    - The findings may reflect selective survival, whereby younger obese people may not have survived to reach the ages studied. Those who did may be genetically protected from cardiovascular disease
- Although those who died had lower BMI values, all subjects have values in the normal range. This suggests that the values developed for the whole population may not be appropriate for assessing risk in the elderly.

Reviewer Comments:

Author-identified limitations:

- *The cohort was initially hospitalized for acute illness and studied for orthostatic hypotension, which limits generalizability*
- *BMI of excluded subjects was not measured. Excluded subjects were of generally poorer health, so their BMI-mortality association may be different from what was observed*
- *Increased mortality among those with lower BMI may be due to pre-existing conditions, especially since BMI was measured only once and not followed over time*
- *Cause of death was abstracted from death certificates, not autopsy records, which may lead to misclassification bias.*

Reviewer-identified limitations:

- *The authors identified the potential for selection bias and limited generalizability, and the risk for this bias seems quite severe. Participants were recruited from among hospitalized patients, so the findings may not reflect BMI-to-mortality associations among healthier older adults. Of the 1,852 screened for the primary cohort study, 1,350 (73%) were either unable to stand or unwilling to cooperate, further calling into question whether the remaining one quarter were truly like the population*
- *The study capitalized on an available cohort. Although this made examining a BMI-to-mortality association straightforward, the entry criteria for the original study may have been overly stringent. Participants had to stand for height and blood pressure measures. Blood pressure isn't relevant to calculating BMI, and methods are available for determining height for people who cannot stand. Given the high fraction of people excluded, the eligibility criteria may not have been appropriate*
- *However, in their final statement, the authors appropriately limited their conclusion to elderly hospitalized patients.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes

1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2. Was the selection of study subjects/patients free from bias? — Yes

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No

3. Were study groups comparable? — Yes

3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A

4. Was method of handling withdrawals described? — Yes

4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A

5. Was blinding used to prevent introduction of bias? — **Yes**

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A

6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described? — **Yes**

6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

7. Were outcomes clearly defined and the measurements valid and reliable? — **Yes**

7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	N/A

7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes

8. **Was the statistical analysis appropriate for the study design and type of outcome indicators?** — Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A

9. **Are conclusions supported by results with biases and limitations taken into consideration?** — Yes

9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes

10. **Is bias due to study's funding or sponsorship unlikely?** — Yes

10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes